FULL TEXT OF CASES (USPQ FIRST SERIES)
In re Bundy, 209 USPQ 48 (CCPA 1981)

In re Bundy

(CCPA)
209 USPQ 48

Decided Feb. 26, 1981
No. 80-591
U.S. Court of Customs and Patent Appeals

Headnotes

PATENTS

1. Patentability -- Utility (§ 51.75)

Pleading and practice in courts -- Burden of proof -- In general (§ 53.131)

Pleading and practice in Patent Office -- Rejections (§ 54.7)

Specification -- Sufficiency of disclosure (§ 62.7)

Burden shifts to appellant to provide rebuttal evidence, where enablement question is whether disclosure of utility in terms of being useful and used in same manner as known series of analogs of prostaglandins is sufficient to satisfy how-to-use requirement of first paragraph of 35 U.S.C. 112, only when Patent Office has adequate support for its challenge to credibility of applicant's statements as to utility.

2. Specification -- Sufficiency of disclosure (§ 62.7)

Disclosure of some activity coupled with knowledge as to use of this activity is necessary to satisfy how-to-use requirement of Section 112.

3. Specification -- Sufficiency of disclosure (§ 62.7)

Situation in which sufficient guidelines as to use are given in disclosure is not same situation as in In re Gardner, 166 USPQ 138; no parallel can be drawn to In re Kirk, 153 USPQ 48, where in present case basic pharmacological activity has been established and not merely presumed from similar molecular structure.

4. Patent grant -- Intent of patent laws (§ 50.15)

Specification -- Sufficiency of disclosure (§ 62.7)

Early filing of application with its disclosure of novel compounds that possess significant therapeutic use is to be encouraged; requiring specific testing of thousands of prostaglandin analogs encompassed by claim in order to satisfy how-to-use requirement of Section 112 would delay disclosure and frustrate, rather than further, interests of public.

5. Pleading and practice in Patent Office -- Rejections (§ 54.7)

Specification -- Sufficiency of disclosure (§ 62.7)

Although holding that appellant has adequately told how to use novel compounds necessarily undercuts best mode rejection founded on lack of enablement, thrust of inquiry is not same for determining satisfaction of further requirement that specification set forth best mode contemplated by inventor for carrying out his invention; satisfaction of best mode requirement of Section 112 is question separate and distinct from question of sufficiency of disclosure to comply with enablement provision; question is one of concealment, i.e., whether applicant has withheld what he considers to be best mode of carrying out his invention; best mode requirement does not require one to obtain further knowledge but only to disclose what one knows or, at least, contemplates.

6. Specification -- Sufficiency of disclosure (§ 62.7)

Inference of withholding of information as to best mode of use cannot be made from appellant's general statements of increased selectivity and narrower spectrum of potency of novel analogs that are conclusions that could be drawn from elementary pharmacological testing of prostaglandin analogs that established basic E-type activity.

Particular patents -- Prostaglandins

Bundy, 3,7-Inter-m-Phenylene-4,5,6-Trinor-2-Decarboxy-2-Hydroxymethyl-9 -Deoxy-9-Methylene-PGF-Type Compounds, rejection of sole claim reversed.

Case History and Disposition:

4,461,917

Appeal from Patent and Trademark Office Board of Appeals.

Application for patent of Gordon L. Bundy, Serial No. 832,329, filed Sept. 12, 1977, division of application, Serial No. 682,848, filed May 4, 1976, issued as U.S. patent No. 4,060,530, Nov. 29, 1977. From rejection of sole claim, applicant appeals. Reversed.

Attorneys:

Robert A. Armitage, Kalamazoo, Mich., for appellant.

Joseph F. Nakamura (Gerald H. Bjorge, of counsel) for Patent and Trademark Office.

Judge:
Before Markey, Chief Judge, and Rich, Baldwin, Miller, and Nies, Associate Judges.

Opinion Text

Opinion By:
Nies, Judge.

This appeal is from the decision of the Patent and Trademark Office (PTO) Board of Appeals (board) affirming the rejection of the sole claim of appellant's application [1] under the first paragraph of 35 USC 112. [2] We reverse.

The appeal raises questions regarding the extent to which new pharmaceuticals must be tested, preceding the filing of an application, in order to satisfy the how-to-use and best mode requirements of §112.

The Invention

The invention relates to a new series of analogs of naturally-occurring prostaglandins [3] which differ from the corresponding known prostaglandins in that these analogs have a methylene group at the C-9 position [4]. Structurally, the compounds may be considered analogs of either E-type prostaglandins (PGEs) in which the methylene group replaces the usual C-9 keto- or oxo-group or of F-type prostaglandins (PGFs) in which the methylene group replaces the C-9 hydroxyl group. Pharmacologically, however, the analogs are related only to PGEs.

The sole claim reads:

131. A prostaglandin analog of the formula
Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

wherein Y_1 is trans --CH=CH--, --C=C--, or --CH_2CH_2;

wherein M_1 is
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or
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wherein R_5 is hydrogen or methyl;

wherein L_1 is

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or a mixture of
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and
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wherein R_3 and R_4 are hydrogen, methyl, or fluoro, being the same or different, with the proviso that one of R_3 and R_4 is fluoro only when the other is hydrogen or fluoro;

wherein g is one, 2 or 3; and

wherein m is one to 5, inclusive.

The Disclosure

The specification of U.S. Patent No. 4,060,534 ('534) has been incorporated by reference to serve as the specification for the present application. The portions of the specification directed to using these novel analogs are pertinent to the issues on appeal.

The background section of the specification contains a detailed description of the uses of various *known* PGE_s. Nine specific biological responses caused by PGE_s, ranging from decreasing blood pressure to inhibiting gastric secretion, are listed. Based on these responses, various pharmacological uses with broad ranges of dosage by various methods of administration are enumerated.

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The use of appellant's novel analogs, which include not only the claimed compounds of this application, but also those claimed in other divisional applications and in '534, is subsequently set forth:

> The novel prostaglandin analogs of this invention correspond to the prostaglandins described above in that the novel prostaglandin analogs exhibit prostaglandin-like activity.
>
> Specifically the 9-deoxy-9-methylene-PGF-type compounds of this invention correspond to the PGE compounds described above, in that these novel 9-deoxy-9-methylene-PGF-type compounds are useful for each of the above-described purposes for which the PGE compounds are used, and are used in the same manner as the PGE compounds, as described above.

> The PGE compounds described above, are all potent in causing multiple biological responses even at low doses. Moreover, for many applications, these prostaglandins have an inconveniently short duration of biological activity. In striking contrast, the novel prostaglandin analogs of this invention are substantially more selective with regard to potency in causing prostaglandin-like biological responses, and have a substantially longer duration of biological activity. Accordingly, each of these novel prostaglandin analogs is surprisingly and unexpectedly more useful than one of the corresponding prostaglandins described above for at least one of the pharmacological purposes indicated above for the latter, because it has a different and narrower spectrum of biological potency than the known prostaglandin, and therefore is more specific in its activity and causes smaller and fewer undesired side effects than when the prostaglandin is used for the same purpose. Moreover, because of its prolonged activity, fewer and smaller doses of the novel prostaglandin analog are frequently effective in attaining the desired result.

The specification includes a disclosure relating to preparation of the compounds generally, and several specific examples. None, however, are compounds within the subgenus claimed in this application.

No example of a specific use of *any* of the disclosed prostaglandin analogs, i.e., setting forth a dosage to achieve a desired response, is given.

The Rejection

The examiner rejected the sole claim under the first paragraph of 35 USC 112 as being "inadequately supported by the instant specification" in that not a single example was directed to one of the claimed compounds. Failure to meet the best mode requirement was also raised on the basis of no exemplification. Reliance on utilities similar to known PGE_s was attacked on the basis of a statement in a "Samuelsson et al. reference" (more correctly, a Rosenthale paper therein) [5] that "small changes in the [prostaglandin] molecule can alter potency or even induce diametrically opposite pharmacologic effects." Thus, the utilities asserted on the basis of those known for structurally analogous compounds were said to be "at best highly speculative."

Before the board the §112 rejection was more specifically explained by the examiner to encompass an inadequate disclosure of: (1) the description of the compounds; (2) the preparation of the same; (3) their use; and (4) the best mode of carrying out the invention. The examiner added that an undue amount of experimentation would be required to prepare the claimed compounds and to determine their utilities.

The board held that the description and how-to-make requirements of the first paragraph of 35 USC 112 were satisfied by appellant's disclosure. It agreed with the examiner, however, that:

> [U]ndue experimentation would be required on the part of one of ordinary skill in the relevant art to determine how to use the compounds claimed. Since we consider the manner of using a compound to be necessarily a part of "the best mode contemplated by the inventor of carrying out the invention", we also agree with the examiner's position that the best mode requirement has not been met.

The challenge raised by the examiner's citation of the Rosenthale paper was deemed reasonable and unrebutted by any factual evidence. The board then added:

> [O]ne of the advantages alleged for the compounds here claimed is that they are more selective than the analogous PGE compounds. This is an express indication

> that not all of the compounds covered by appellant's claims will induce the same biological responses.

Accordingly, the board affirmed the examiner's rejection of the sole claim to the extent it was based on the how-to-use and best mode requirements of §112.

Opinion

How-to-Use

The enablement question present here is whether the disclosure of utility in terms of being useful and used in the same manner as known PGEs is sufficient to satisfy the how-to-use requirement of the first paragraph of 35 USC 112.

[1] The PTO must have adequate support for its challenge to the credibility of applicant's statements as to utility. Only then does the burden shift to appellant to provide rebuttal evidence. In re Gardner, 475 F.2d 1389, 177 USPQ 396 (CCPA 1973); In re Marzocchi, 58 CCPA 1069, 439 F.2d 220, 169 USPQ 367 (1971). We must consider the Rosenthale paper in its entirety in determining the reasonableness of the doubt raised by the authors' conclusory statement relied on by the examiner, and in so doing see no specific evidence that structural variations of PGEs cause opposite pharmacologic effects. The tests reported by Rosenthale do indicate shifts in PGF_{2a} activity from bronchoconstrictor to broncodilator concomitant with structural changes. For PGE Rosenthale shows only variations in potency, a matter of degree of activity. Accordingly, we do not agree that Rosenthale is sufficient support for the examiner's position that the subject analogs, related as they are to PGE_s in pharmacological activity, may not be useful at all to achieve a particular response.

The board focused on another reason for challenging the disclosure as non-enabling. Appellant's disclosure of increased "selectivity" of the novel analogs was taken as an express indication that it was uncertain "which compound will induce which biological responses * * *," thus virtually ensuring that an undue amount of experimentation would be required to use the invention. The ranges of dosage for known PGEs, assuming their applicability to appellant's analogs, were said to be very broad and would, in any event, provide little guidance in determining dosages for the more selectively functional claimed analogs.

Appellant contends that the disclosure teaches that *all* novel compounds exhibit *each* of the enumerated pharmacological uses. The increased selectivity is said to be with respect to the potency for each activity, not to the existence of that biological activity. Any contrary interpretation of the specification is strongly denied. As far as determining dosages for the novel analogs is concerned, it is urged that the experimentation needed to ascertain proper levels for various responses would not be undue, but rather would lie well within the ability of one of ordinary skill in the art. At most, appellant states, the question is whether the determinations would be extended, not undue.

[2] We have no difficulty with appellant's interpretation of "selectivity". In the pertinent section, previously quoted, it is clearly stated that the novel compounds are "useful for *each* of the above-described purposes for which the PGE compounds are used" (emphasis added). This can only reasonably be read as teaching that *each* compound can be used for *each* and every one of the aforesaid biological responses. Appellant's further statements that the novel analogs are "substantially more selective with regard to potency" or "more specific in its activity" because of a "different and narrower spectrum of biological potency," does not negate the asserted usefulness for each purpose. There is no requirement that all have the same degree of activity for each use. What is necessary to satisfy the how-to-use requirement of §112 is the disclosure of some activity coupled with knowledge as to the use of this activity. In re Gardner, 475 F.2d at 1392, 177 USPQ at 398.

Thus the remaining question is whether appellant's disclosure is sufficient to enable one of ordinary skill in the art to use these novel analogs. No specific examples of dosages for human use or even animal tests are given for the novel compounds per se. Appellant's counsel stated at oral argument that all that had been established at the time of filing the application was the basic pharmacology for these compounds. Appellant's specification discloses that these compounds possess activity similar to E-type prostaglandins. As to the latter, dosages are disclosed, albeit expressed in very broad ranges.

[3] We do not consider that one of ordinary skill in the art would not know how to use these novel analogs to determine the specific dosages for the various biological purposes. We are persuaded that sufficient guidelines as to use are given in the disclosure here. This is not the same situation as in In re Gardner et al., 57 CCPA 1207, 427 F.2d 786, 166 USPQ 138 (1970). Here

only the compounds themselves are being claimed, not their therapeutic use. Nor can a parallel be drawn to In re Kirk, 54 CCPA 1119, 376 F.2d 936, 153 USPQ 48 (1967), the basic pharmacological activity having been established in this case, not merely *presumed* from similar molecular structure.

[4] Early filing of an application with its disclosure of novel compounds which possess significant therapeutic use is to be encouraged. Requiring specific testing of the thousands of prostaglandin analogs encompassed by the present claim in order to satisfy the how-to-use requirement of §112 would delay disclosure and frustrate, rather than further, the interests of the public.

Accordingly, we are satisfied that the how-to-use requirement of the first paragraph of §112 has been adequately complied with by appellant's disclosures.

Best Mode

[5] Turning to the best mode issue, we agree with appellant that this rejection was founded on a lack of enablement by both the examiner and the board. Our holding that appellant has adequately told how to use the novel compounds necessarily undercuts this position. However, we do not agree that the thrust of the inquiry is the same for determining satisfaction of the further requirement that the specification shall set forth the best mode contemplated by the inventor of carrying out his invention.

Satisfaction of the best mode requirement of §112 is a question separate and distinct from the question of the sufficiency of the disclosure to comply with the enablement provision. In re Gay, 50 CCPA 725, 731, 309 F.2d 769, 772, 135 USPQ 311, 315 (1962). The question is one of concealment, i.e., whether an applicant has *withheld* what he considers to be the best mode of carrying out his invention. The best mode requirement does not require one to obtain further knowledge but only to disclose what one knows or, at least, contemplates.

The Solicitor argued that concealment may be inferred. Quoting the disclosure in the specification that each analog is "surprisingly and unexpectedly more useful than one of the corresponding prostaglandins * * * for at least one of the pharmacological purposes * * *," he urges that appellant must have had test results to substantiate this statement and this data should have been disclosed. The alleged withholding of information on which these general statements were made is said to render the quality of disclosure so poor that it effectively results in concealment, citing In re Sherwood, 613 F.2d 809, 816, 204 USPQ 537, 544 (CCPA 1980).

[6] Were we to see merit in the Solicitor's position fairness would require providing appellant with the opportunity to present evidence in rebuttal. However, we do not find it necessary for appellant to assume this burden of proof. We can infer no withholding of information as to the best mode of use from appellant's general statements of increased selectivity and narrower spectrum of potency for these novel analogs, conclusions which could be drawn from the elementary pharmacological testing of the analogs which established the basic E-type activity.

Accordingly, we reverse the holding that the best mode requirement has not been satisfied.

Conclusion

The board's affirmance of the rejection of appellant's sole claim under both the how-to-use and the best mode requirements of the first paragraph of §112 is *reversed.*

Reversed.

Footnotes

Footnote 1. Serial No. 832,329, filed September 12 1977, for 3, 7-Inter-m-Phenylene-4, 5, 6-Trinor-2-Decarboxy-2-Hydroxymethyl- 9 -Deoxy-9-Methylene-PGF-Type Compounds. The application is a divisional application of Ser. No. 682,848, filed May 4, 1976, issued as U.S. Patent No. 4,060,534 on November 29, 1977.

Footnote 2.

The first paragraph of §112 reads:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Footnote 3. Natural prostaglandins are found in mammalian tissues and have varied pharmacologic uses including the treatment of hypertension, ulcers and asthma, and the interruption of pregnancy. In naming the prostaglandins, the prefix PG is followed by a letter designating the oxidation state of the cyclopentane ring; thus arise the series PGA, PGE, PGF, etc. The numeral subscript refers to the number of double bonds in the side chain. 1 D. Lednicer & L. Mitscher, The Organic Chemistry of Drug Synthesis, 23-27 (1977).

Footnote 4. A typical example of a naturally-occurring prostaglandin is PGE 2which structurally is represented:
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Footnote 5. Cited by the examiner as: Samuelsson et al., Advances in Prostaglandin and Thromboxane Research, Vol. 1 (1976) 488-491.

Appellant has pointed out that the work relied upon is a paper by Rosenthale et al. entitled "Actions of Prostaglandins on the Respiratory Tract of Animals," pp. 477-493 included in the above book, edited by Samuelsson et al. Henceforth we shall refer to this reference as the Rosenthale paper.

- End of Case -

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